EMA/401494/2023

European Medicines Agency decision

P/0442/2023

of 27 October 2023

on the acceptance of a modification of an agreed paediatric investigation plan for tovorafenib (EMEA-002763-PIP01-20-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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on the acceptance of a modification of an agreed paediatric investigation plan for tovorafenib (EMEA-002763-PIP01-20-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0500/2020 issued on 22 December 2020,

Having regard to the application submitted by Day One Biopharmaceuticals, Inc on 24 May 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 8 September 2023, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for tovorafenib, tablet, age-appropriate oral formulation, oral use, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to Day One Biopharmaceuticals, Inc, 2000 Sierra Point Parkway Suite 501, 94005-1874 - Brisbane, United States.

EMA/PDCO/260417/2023
Amsterdam, 8 September 2023

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-002763-PIP01-20-M01

Scope of the application

Active substance(s):

Tovorafenib

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of paediatric low grade glioma

Pharmaceutical form(s):

Tablet

Age-appropriate oral formulation

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Day One Biopharmaceuticals, Inc

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Day One Biopharmaceuticals, Inc submitted to the European Medicines Agency on 24 May 2023 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0500/2020 issued on 22 December 2020.

The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 10 July 2023.

Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of paediatric low grade glioma

The waiver applies to:

- The paediatric population from birth to less than 6 months of age;
- tablet, age-appropriate oral formulation, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition:

Treatment of paediatric low grade glioma

2.1.1. Indication(s) targeted by the PIP

Treatment of relapsed or refractory patients with low grade glioma harbouring BRAF fusion

Treatment of patients newly diagnosed with unresectable or sub-totally resected low-grade glioma harbouring BRAF fusion

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 6 months to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Tablet, age-appropriate oral formulation

2.1.4. Measures

Area	**Description**
Quality-related studies	**Study 1** Development of an age-appropriate oral formulation.
Non-clinical studies	Not applicable.
Clinical studies	**Study 2 (PNOC014)** *deleted during EMEA-002763-PIP01-20-M01* **Study 3 (FIREFLY-1)**

	Open-label, single arm trial, to evaluate pharmacokinetics, safety and activity of DAY101 in children from 6 months to less than 18 years of age (and adults up 25 years) with RAF-altered, recurrent or progressive low grade glioma. **Study 4 (FIREFLY-2)** Randomised controlled, open label trial to evaluate safety and efficacy of DAY101 in children from 6 months to less than 18 years of age (and adults up to 25 years) with newly diagnosed unresectable or sub-totally resected low-grade glioma harbouring an activating RAF alteration.
Extrapolation, modelling and simulation studies	**Study 5** Modelling and simulation study to confirm or modify the paediatric posology in children from 6 months to less than 18 years of age with low grade glioma.
Other studies	Not applicable.
Other measures	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By July 2030
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.